

# Hindered Transport in Composite Hydrogels

by  
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## ABSTRACT

The ultimate goal of this research was to develop a greater understanding of the structural components needed to describe transport within the glomerular basement membrane (GBM). Specifically, dimensionless diffusive and convective hindrance factors were investigated by measuring macromolecular permeability through synthetic, two-fiber, agarose-dextran hydrogels at very small or very high  $Pe$ , respectively. By comparing diffusion and convection in the synthetic hydrogel with corresponding measurements in isolated rat GBM, further insight regarding the structure responsible for transport through the GBM was gained. In order to compare diffusive hindrances in the synthetic gels with those in isolated GBM, partitioning in agarose-dextran hydrogels was also examined. Additionally, hindered transport theories were tested.

In studying diffusion, partitioning, and convection, macromolecules with Stokes-Einstein radii ( $r_s$ ) ranging from 2.7 to 5.9 nm were used. Gels with agarose volume fractions of 0.040 and 0.080 were studied with dextran volume fractions (assuming dextran acts as a fiber) ranging from 0 to 0.0076 and 0 to 0.011, respectively. For the diffusion studies, two globular proteins (ovalbumin and bovine serum albumin) and three narrow fractions of Ficoll, a spherical polysaccharide, were used. For the partitioning and convection studies, four narrow fractions of Ficoll were used.

Diffusivities of fluorescein-labeled macromolecules were measured in dilute aqueous solution ( $D_\infty$ ), agarose gels ( $D_a$ ), and agarose-dextran composite gels ( $D$ ) using fluorescence recovery after photobleaching. For both agarose concentrations, the Darcy permeability ( $\kappa$ ) decreased by an order of magnitude as the dextran concentration in the gel was increased from zero to its maximum value. For a given gel composition, the relative diffusivity ( $D/D_\infty$ ) decreased as  $r_s$  increased, a hallmark of hindered diffusion. For a given test molecule,  $D/D_\infty$  was lowest in the most concentrated gels, as expected. As the dextran concentration was increased to its maximum value, 2-3 fold decreases in relative diffusivity resulted for both agarose gel concentrations. The reductions in macromolecular diffusivities caused by incorporating various amounts of dextran into agarose gels could be predicted fairly accurately from the measured decreases in  $\kappa$ , using an effective medium model. This suggests that one might be able to predict diffusivity variations in complex, multicomponent hydrogels (e.g. those in body tissue) in the same manner, provided that values of  $\kappa$  can be obtained.

Equilibrium partition coefficients ( $\Phi$ , the concentration in the gel divided by that in free solution) of fluorescein-labeled Ficolls in pure agarose and agarose-dextran composite gels were measured as a function of gel composition and Ficoll size. As expected,  $\Phi$  generally decreased as the Ficoll size increased (for a given gel composition) or as the amount of dextran incorporated into the gel increased (for a given agarose concentration and Ficoll size). The decrease in  $\Phi$  that accompanied dextran addition was predicted well by an excluded volume theory in which agarose and dextran were both treated as rigid, straight, randomly positioned and oriented fibers. Modeling dextran as a spherical coil within a fibrous agarose gel produced much

less accurate predictions. The diffusional permeabilities of these gels were assessed by combining the current partitioning data with relative diffusivities, or diffusive hindrance factors ( $K_d = D/D_\infty$ ), reported previously. The values of  $\Phi K_d$  for a synthetic gel with 8.0% agarose and 1.1% dextran (by volume) were found to be very similar to those for the GBM in vitro, which also has a total solids content of ~10%.

The sieving coefficient ( $\Theta$ ), or the ratio of the macromolecular downstream concentration to that at the upstream membrane surface, was measured in high Peclet number flow where  $\Theta = \Phi K_c$ . The convective hindrance factor ( $K_c$ ) is the macromolecular velocity in the gel due to bulk flow divided by that of the superficial fluid. The measured sieving coefficients of four narrow fractions of Ficoll in agarose and agarose-dextran composite gels decreased with each addition of dextran. For a given gel composition,  $\Theta$  generally decreased as the size of the macromolecule increased. While theories describing hindered convection in random fiber matrices have yet to be developed,  $\Phi K_c$  seems to correlate well with  $\kappa$ , for a given  $r_s$ , based on the predictions of parallel fiber theory for a number of different macromolecules and a variety of gel compositions. The inherent differences in averaging between the observable partition and sieving coefficients in gels with fiber spacing heterogeneity result in large apparent  $K_c$ , as substantiated by examination of hindered transport in parallel fiber media. Comparison of  $\Phi K_c$  in agarose-dextran synthetic gels and isolated GBM continues to support the idea that the GBM transport properties can be explained by its mixture of thick and thin fibers, rather than its precise chemical composition.

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